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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,385	11/06/2000	Michael Petersen	A33251	3514

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EXAMINER	
MARX, IRENE	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/622,385	PETERSEN ET AL.	
	Examiner	Art Unit	
	Irene Marx	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 5/7/04.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 8-16 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 8-16 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 06 August 2000 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/7/04 has been entered.

Claims 1-7 are cancelled by the amendment filed 9/8/03.

Claims 8-16 are being considered on the merits.

The drawing page comprising Fig. 1 and 2 is acknowledged and accepted. At page 7 the Brief Description of Drawings should be labeled appropriately.

To update the record, the specification should be amended to read: --This application was filed under 35 USC 371 as the national phase of PCT/EP99/01017 filed February 18, 1999--.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is inconsistent in the recitation of "4,4,4-trifluoro..." at line 2 and "a trifluoro" at line 12. The "trifluoro" compound also appears to be a "4,4,4-trifluoro" compound.

Claim 8 is confusing in the recitation of "a microcoorganisms" at line 22 followed by "the microorganisms express" at line 23. Clarification is required. Claim 9 also recites "microorganisms".

Claim 11 fails to find proper antecedent basis in claim 9 for *"Escherichia coli"*.

Claims 13 and 14 are confusing in that it is uncertain whether "the process" is the process of transformation or the bioconversion.

Claims 13 and 15 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may not depend on another multiple dependent claim. Moreover, the correct language is "any one of". See MPEP § 608.01(n).

Claims 8-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a process of biotransformation of a 4,4,4-trifluoroacetic acid with multitude of *Escherichia* strains or cell-free extracts derived therefrom that express an enzyme which enantioselectively reduces the trifluoroacetoacetic acid to produce the required product or which is transformed with a gene encoding an enzyme which reduces a carbonyl function or with an *Escherichia coli* which is transformed with a gene encoding a glucose dehydrogenase. In contrast, the specification only provides guidance for this biotransformation using strains *E. coli* JM109 and DH5 each transformed with two specific plasmids pKAR and pKKDGH using specific promoters and selection markers. No guidance is presented for the evaluation or production of other *Escherichia* strains or cell-free extracts thereof which express an enzyme that effects the required enantioselective process of biotransformation. Similarly, no guidance is presented for the evaluation or production of strains or cell free extracts thereof wherein the *Escherichia are* transformed with a gene encoding an enzyme which reduces a carbonyl function or wherein the *Escherichia coli* is transformed with a gene encoding a glucose dehydrogenase to effect the required biotransformation. The respective suitable enzymes and genes thereof as well as expression systems suitable for all strains are not identified.

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the claimed invention.

See University of California v. Eli Lilly and Co., 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

See Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021 and 1027, (Fed. Cir. 1991) at page 1021, where it is taught that a gene (or promoter) is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA

sequence), and at page 1027, where it is taught that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof.

Claims 8-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for strains of *Escherichia coli* transformed with plasmids pKAR and pKKGDH, does not reasonably provide enablement for the use of any *Escherichia* that express enzymes or transformed with a glucose dehydrogenase gene from any organism or cell free extracts thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The production or selection and identification of *Escherichia* microorganisms that naturally produce or which are transformed with an unidentified carbonyl reductase or with any glucose dehydrogenase gene from any organism having the required capability is unpredictable. The specification as-filed does not provide sufficient guidelines or teachings for the identification of strains or the construction of recombinant microorganisms having the required ability, since the only genes required for the process identified and isolated are the reductase gene from *Sporolobomyces salmonicolor* and the glucose dehydrogenase gene *Bacillus megaterium.* The identification and isolation of other strains of *Escherichia* or of other genes for enzymes specifically capable of the required enantioselective biotransformation is not disclosed. The teachings provided in the as-filed specification would not have enabled one skilled in the art to "make" recombinant *Escherichia* or isolate specific *Escherichia* strains capable of expression of enzymes for the enantioselective biotransformation in the claim designated methods. The guidance provided in the specification is not adequate to lead such persons toward success in making and using all of the *Escherichia* microorganisms and cell-free extracts to be used in the enantioselective process encompassed by the claims in a predictable manner. It is apparent that applicant is offering an "invitation to experiment" to those skilled in the art to perform various techniques and to determine for themselves whether they have obtained a suitable *Escherichia* naturally or by recombinant techniques having the claimed capabilities. See Genentech, Inc. v Novo Nordisk A/S., 42 USPQ2d, 1001, 1005 (Fed. Cir. 1997) ("Tossing out the mere germ of an idea does not constitute an enabling disclosure"). Also, In re Scarbrough, 182 USPQ 298, 302 (CCPA 1974) ("It is not enough that a person skilled in the art, by carrying out investigations

along the line indicated in the instant application, and by a great amount of work eventually might find out how to make and use the instant invention. The statute requires the application itself to inform, not to direct others to find out for themselves. In re Gardner et al., 166 USPQ 138 (1970)").

Undue experimentation would be required to practice the invention as claimed due to the quantity of experimentation necessary to identify the *Escherichia* strains and/or genes required and attain expression of the required enzymes for enantioselective reduction of a specific trifluoro compound; limited amount of guidance and limited number of working examples in the specification directed to finding other members within *Escherichia* and/or identification of suitable genes and transformation therewith as well as effecting expression of the enzymes encoded thereby in *Escherichia* for enantioselective reduction of a specific trifluoro compound; the unpredictable nature of an invention directed to the use of unidentified *Escherichia* microorganisms and cell extracts thereof, protocols for the identification of which is not disclosed with any particularity for enantioselective reduction of a specific trifluoro compound; the unpredictability of biological systems, as argued by applicants, and breadth of the claims directed to the use of natural or recombinant microorganisms expressing unidentified genes for enantioselective reduction of a specific trifluoro compound. In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Thus, the scope of the claims is not commensurate with the teachings of enablement of the specification.

Response to Arguments

Applicant argues persuasively in the last Response, at page 9, that due to the unpredictability of biological systems, the reductase disclosed by Kula from *Candida parapsilosis*, having an extremely broad substrate spectrum, would not have provided one skilled in the art with a reasonable expectation that such a reductase of *Candida parapsilosis* could be successfully cloned and expressed in *E. coli*. Applicant does not even address cloning and expression in the genus *Escherichia* as a whole.

Therefore the rejection is deemed proper and it is adhered to.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Irene Marx whose telephone number is (571) 272-0919. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Irene Marx

Irene Marx
Primary Examiner
Art Unit 1651